Environmental Health Perspectives
Vol. 9, pp. 325–326, 1974

Commentary

Use of Experimental Animals

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I shall deal briefly this morning with three topics: (1) the different species and strains of animals to be employed in experimental studies of bowel cancer with asbestos; (2) combinations of carcinogens; and (3) the difficult and debatable tumors that one sees in experimental animals.

I am glad to see that in South Africa baboons are also being used. Frequently Wistar rats are used or rats of no particular pedigree at all, but there is a strain of rat, the Buffalo strain, that spontaneously develops mesothelioma of the tunica vaginalis testis. The mesothelioma in some animals spreads upwards into the abdominal cavity. It is advantageous to use an animal that develops spontaneously the tumor that you wish to induce. Then if the agent is effective you increase the percentage of animals with the tumors and/or you shorten the latent period. Other species should be tried besides the rat and the baboon. Clayson reported many years ago *(1)* that when five known carcinogens that produce cancer of the bladder in man were tested in four or five species of animals, the animals reacted differently. Individual chemicals might produce only cancer of the bladder; cancer of the bladder and cancer at other sites; or cancer at other sites but not in the bladder, or no cancer at all. One of the most potent—β-naphthylamine—produced bladder cancer in dogs but not in rats, rabbits, or guinea pigs, and was only a weak carcinogen for mice. So I think it is very important to select different strains and species of animals for experimentation.

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Now the question came up about bowel cancer and its possible relationship to asbestos exposure. To induce cancer of the bowel in animals requires very specific carcinogens and frequently very specific regimens. For example, foam rubber injected into the peritoneal cavity induces cancer of the cecum. Cycasin, which comes from the nut of the primitive palm tree, the cycad tree, produces cancers in the ascending colon. Radioactive yttrium, because of its slow passage through the bowel is held up longest in the descending colon and the radiation is more prolonged and therefore more intense there; therefore cancers develop at that site. Benzidine produces cancer of the rectum. There are thus different regimens and types of carcinogens that one uses to induce cancers at specific sites in the intestine. I believe that in human beings whatever produces cancer of the bowel at each different site must be very highly specific. Combinations of carcinogens must be important because we human beings carry around with us a large complement of carcinogens. We are continually replenishing them by new exposure through the alimentary tract, respiratory tract and skin. It is known, for example, that two weak carcinogens may potentiate each other so as to produce many more tumors than either alone. Noncarcinogenic fibers may attract chemical carcinogens. I sewed a cotton thread into the abdominal wall of rats and fed them the chemical carcinogen *N,N'*-2,7-fluorenylenebisacetamide (2,7–FAA). Among the tumors that arose in those rats were sarcomas right around that thread. Now the thread itself was not carcinogenic, but by giving by mouth the 2,7–FAA and having the thread in the ab-

dominal wall, the rats developed sarcomas. Could it be that tumors would develop, at deposits sites of asbetos fibers, in a person who then ingested a chemical carcinogen? That is pure speculation, but one might test it experimentally. Should one use only perfectly healthy animals in attempts to induce bowel cancer? Consider the human population. Many Americans are not well, they are sick. Some have divertica, diverticulitis, ulcerative colitis, polyps, and enteritis. In experiments one should duplicate these lesions in the experimental animals, and then feed them asbestos.

Finally a word about the types of lesion that one sees in experimental animals. Many of them are more difficult to diagnose and less well understood than are lesions of human beings. For example, we at the Registry, see cases of identical tumors of the ovaries of mice which some have diagnosed as mesotheliomas or as papillary cystic carcinomas. Another set of confusing lesions are those induced in the lungs of rats by a variety of agents. Such lesions may be represented by alveogenic tumor, mucinous adenocarcinoma, squamous-cell carcinoma, simple alveolar cell proliferation, pulmonary adenomatosis, squamous metaplasia of the alveoli and bronchi, and fibrosis, inflammation, bronchicectasis and cellular metaplasia. So in any planned experiment with asbestos it is well to establish a reliable group of pathologists with competent supporting personnel. The end results of most such experiments depend upon correct pathologic evaluation.

REFERENCE

1. Clayson, D. B. Chemical Carcinogenesis, Little, Brown, Boston, 1962, p. 303.